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NOTIFICATION OF TRANSMITTAL OF COPIES OF TRANSLATION OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 72.2)

"Paraphiersee"

From the INTERNATIONAL BUREAU

To:

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Date of mailing (day/month/year) 07 June 2001 (07.06.01)	
Applicant's or agent's file reference 1998/103	**IMPORTANT NOTIFICATION**
International application No. PCT/EP99/08042	**International filing date** (day/month/year) 23 October 1999 (23.10.99)
Applicant LTS LOHMANN THERAPIE-SYSTEME AG et al	

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. Transmittal of the copy of the translation to the elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AU,CA,CN,JP,KR,NZ,PL,US

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

EP,BR,CZ,HU,IL,IN,MX,RU,TR,ZA

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
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1211 Geneva 20, Switzerland

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Translation

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

8

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
LTS 1998/103 WO		
International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/EP99/08042	23 October 1999 (23.10.99)	03 November 1998 (03.11.98)

International Patent Classification (IPC) or national classification and IPC

A61K 9/70

Applicant

LTS LOHMANN THERAPIE-SYSTEME AG

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15 May 2000 (15.05.00)	23 February 2001 (23.02.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP99/08042

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☒ the description, pages 1-11, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. 1-50, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 19-37,50

because:

☒ the said international application, or the said claims Nos. 19-37,50 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See annex

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III

1. Claims 19-37 and 50 relate to a subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, a report is not established for the industrial applicability of the subject matter of these claims (PCT Article 34(4)(a)(i)).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3-6,16,17,18,19-37,41-43	YES
	Claims	1,2,7-15,38-40,44,46-49,50	NO
Inventive step (IS)	Claims		YES
	Claims	3-6,16,17,18,19-37,41-43	NO
Industrial applicability (IA)	Claims	1-18,38-49	YES
	Claims		NO

2. Citations and explanations

1. The report makes reference to the following documents:

D1: US-A-4 767 402

D2: WO-A-90/01971

D3: SHOZO MIYAZAKI ET AL, CHEMICAL AND PHARMACEUTICAL BULLETIN, JP, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, Vol. 40, No. 10, 1 October 1992 (1992-10-01), pages 2826-2830, XP000324877 ISSN: 0009-2363.

1.1 D1 discloses the use of ultrasound to improve the transdermal administration of drugs (column 2, lines 29-34). Ultrasound is used directly after the drug has been administered, the latter via an aqueous or inorganic gel. It is also possible to release the drug via a plaster containing the active substances (column 4, line 12 - column 5, line 31; Claims 1-8). The ultrasound treatment does not correspond to the ultrasound treatment in the application (Claims 2, 6-13, 20, 24-33). When manitol or insulin were tested on rats, the release of the active ingredients following application was observed over a fairly long period of time (see Ex. 2 and in particular Fig. 4).

1.2 D2 discloses how ultrasound can be used to improve the release of drugs in the inside of the mouth via the mouth mucous membrane (claims, p. 6, line 19 - p. 10, line 22; p. 8, line 19 - p. 9, line 24; Claims 1-15).

1.3 D3 discloses the effects of an ultrasound treatment during a transdermal dosage of indomethacin. An ointment is applied and then the transfer of the drug with and without the application of ultrasound is determined (Fig. 1 - 3; Tables I-III; see also the abstract). The treatment thus comprises an initial phase with the application of ultrasound and a longer phase in which the ointment remains on the skin. The influence of the duration of the ultrasound treatment on the transfer of the active substances was also examined. With applications of longer than 20 minutes the transfer was weaker than with shorter applications (Table III).

2. Novelty (PCT Article 33(2))

2.1 The present application comprises the independent Claims 1 (use), 19 (method) and 50 (use). The feature common to all the claims is the transdermal administration of an active substance.
Administration comprises an initial phase in which ultrasound treatment is carried out and a subsequent longer phase without ultrasound treatment.
Claim 38 concerns the device for carrying out the method.

2.2 Independent Claim 1
The subject matter of independent Claim 1 is anticipated by D3 (see point 1.3).

The same objection applies to Claims 2 and 7-15 which are dependent on Claim 1.

2.3 Independent Claim 19

The subject matter of independent Claim 19 and that of Claims 20-37 which are dependent thereon is not anticipated by the cited prior art.

2.4 Independent Claim 38

The subject matter of Claim 38 is anticipated by D1, D2 and D3 (see 1). The same also applies to Claims 39-41 (D1), 44 (D3) and 46-49 (D1 and D2) which are dependent thereon.

The applicant's attention is drawn to the fact that the claim concerns a device which must be suitable for the purpose indicated.

Furthermore, in the opinion of the Examining Authority, "TTS" (see p. 6, lines 5-10 of the description) "a device or administration method containing a medical substance..." includes all systems that contain a medical substance and can be applied to the skin, for example, also ointments. The systems in D2 can also be used transdermally (p. 8, line 19 - p. 9, line 12).

2.5 Independent Claim 50

The subject matter of independent Claim 50 is anticipated by D3.

3. Inventive step (PCT Article 33(3))

3.1 Plaster systems for dosing active substances are generally known in transdermal therapy. These plaster systems are usually worn in a longer phase. It is known from D1-D3 that ultrasound can be used to reduce the lag-time in transdermal/transbuccal

therapy (see 1). D1 and D2 indicate in particular that the known plaster systems can be used in ultrasound treatment. With respect to D1, it is therefore considered obvious for a person skilled in the art seeking to achieve a shorter lag-time to begin the normal application method of plaster/transdermal systems with an ultrasound treatment.

It is not apparent at present what surprising effect can be achieved by using a plaster containing an active substance or composition more specific than that named in D1. This objection applies to all of the claims which are not anticipated in a manner that is prejudicial to novelty.

4. Industrial applicability (PCT Article 33(4))

4.1 The subject matter of Claims 38-49 meets the requirements of PCT Article 33(4).

4.2 The PCT does not contain uniform criteria for assessing the industrial applicability of Claims 1 to 18 in their present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognise the industrial applicability of claims to the medical use of a compound; it does, however, allow claims to the first medical use of a known compound or to the use of such a compound in the manufacture a drug for a new medical application.